## REMARKS

Claims 1-16, 20 and 21 are active.

As the claims are not amended in this filing, for reference, Claim 1, in part, reads:

> A method of treating coronary obstruction or peripheral vasoconstriction in a patient in need thereof, the method comprising administering an effective amount of a methylene amide of Formula (I) to treat coronary obstruction or peripheral vasoconstriction in the patient . . .

Applicants thank the Examiner for withdrawing all of the prior rejections.

To the new rejection to allege that the claims would have been obvious in view of Liu in view of Sowers (*Hypertension* 2001) and Parissis (*Int J Cardio* 2002), Applicants respectfully disagree.

Sowers and Parisssis are relied upon for their teachings correlating cardiovascular disease with diabetes (Sowers) and vasoconstriction with hypertension (Parissis). Based simply on these correlations and that Liu teaches compounds useful for treating a variety of diseases, including diabetes, the Examiner concludes that one would have administered the compounds to diabetic patients, which would in turn treat coronary obstruction and peripheral vasoconstriction.

Applicants respectfully disagree that the combination of art renders the claims *prima facie* obvious. That is, while under U.S. law, "obvious to try" can be sufficient motivation for one to try to do something, the analysis does not end as there must also have been a reasonable expectation of success. (see, e.g., MPEP 2145).

Even if what is alleged in the rejection was obvious to try, Applicants disagree that there would have been a reasonable expectation of success without first having had performed the experiments shown in the present specification. The missing evidence from the cited publications must therefore lead only to the conclusion that the claims were not obvious. Once this data was available, and only then, could one have a reasonable

expectation of success that compounds within the scope of the claims would work for the treatment of coronary obstruction or peripheral vasoconstriction.

Further, it should be noted that Sowers teaches that cardiovascular diseases is a complication of diabetes and that these two chronic diseases frequently co-exist. Sowers provides information on how specific antihypertensive therapeutic programs can impact the progression of diabetes. On the contrary, the object of the present application is the treatment of cardiovascular disorders using an anti-diabetic agent.

The rejection refers to the following sentence in Sowers: "each pathophysiological disease entity, although independent in their own natural history, serves to exacerbate the other." Nevertheless, this does not provides any evidence that administering one drug to treat diabetes would also treat cardiovascular disorders and the other way around.

Although Sowers establishes that ACE inhibitors may impact the progression of diabetes (see in particular HOPE trial on page 1055) Sowers does not provide any indication as whether an antidiabetic agent, like the compounds of the present application, would impact cardiovascular diseases.

Additionally, Sowers explains the effect of ACE inhibitor to diabetes at the cellular level, through a specific pathway involving angiotensin II and Pi3K (see on page 1056 second paragraph). These biological entities are completely distinct from PTP1 B, which is the biological target of the compounds of the present application.

Therefore, in view of Sowers' document, it is not obvious to one skilled in the art that administering compounds described in Liu would automatically treat cardiovascular diseases. A reasonable expectation of success to treat cardiovascular disorders with PTP1B inhibitors has not been established as no biological link is established between PTPIB and cardiovascular disorders.

Based on these considerations, the teaching of Parissis, as peripheral vasoconstriction is associated with hypertension, is not relevant.

Withdrawal of the rejection is requested.

A Notice of Allowance for all pending claims is also requested.

Respectfully submitted,

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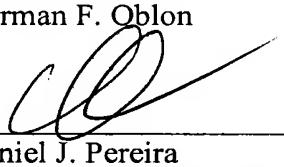

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